INFERTILITY FOR THE PRIMARY CARE PROVIDER

Top Ten Myths

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NOTHING TO DISCLOSE

The top ten myths

Educational Objectives

1. Review the basic workup of the infertile couple.
2. Gain better understanding of the uses of modern modalities to document ovulation.
3. Understand the costs of advanced infertility treatments.
4. Gain insight into the medical coverage of these treatments.

1. Day 3 FSH is important
   - Not by itself
   - Day 3 Estradiol is just as important
   - Less than 80 is good
   - Less than 60 is better
   - AMH may be able to replace both (0.9-9.5)

CD3 FSH

- FSH (mIU/ml)
  - <10 (7-12) Normal
  - 10-20 Less fertile
  - >20 “Donor eggs”
  - >40 Menopause
- Variable from cycle to cycle
- Does not give long term prognosis
- 2 babies with FSH 100

10. IVF docs are all the same
Cycle Day 3 Estradiol

Comparison of previously published studies evaluating the prognostic value of E2 in patients undergoing ART cycles in the current study.

<table>
<thead>
<tr>
<th>Study</th>
<th>ART cycle</th>
<th>E2 (ng/ml)</th>
<th>ART cycles</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis et al, 1995</td>
<td>352</td>
<td>&gt;200</td>
<td>202</td>
<td>Decreased pregnancy rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;100</td>
<td>88</td>
<td>Decreased miscarriage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;75</td>
<td>98</td>
<td>No pregnancy</td>
</tr>
<tr>
<td>Samuels et al, 1995</td>
<td>291</td>
<td>&lt;200</td>
<td>20</td>
<td>Decreased ovulation rate, increased pregnancy rate</td>
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<tr>
<td></td>
<td></td>
<td>&gt;200</td>
<td>15</td>
<td>No pregnancy</td>
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<tr>
<td>Jones et al, 1996</td>
<td>27</td>
<td>&gt;400</td>
<td>96</td>
<td>Decreased ovulation rate, increased miscarriage rate, not in pregnancies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;200</td>
<td>77</td>
<td>Decreased implantation and pregnancy rates only in patients of 45 years</td>
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<tr>
<td>Pandis et al, 2000</td>
<td>144</td>
<td>&lt;20</td>
<td>200</td>
<td>Increased implantation rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;20</td>
<td>98</td>
<td>Increased pregnancy rate</td>
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1. Total number of ART cycles analyzed in the published article.
2. Total number of ART cycles above the published threshold E2 level.

AMH: Anti-Mullerian Hormone

- AMH can be run at any point in the cycle
- AMH can be used to predict poor prognosis
- Can also be used to predict ovarian hyperstimulation syndrome
- May be useful in dosing infertility meds
- May test while patient is on OCP, therefore useful in egg donors

2. BBTs can predict ovulation

- Inexpensive
- Good 40 years ago
- Studies find 15 to 40% correlation with ovulation
- Increases stress
- Not reproducible
- Occurs after ovulation

2. Urinary LH Kits don’t work

<table>
<thead>
<tr>
<th>Kit</th>
<th>Price Response</th>
<th>Laboratory</th>
<th>50 Infertile Lab Cycles</th>
<th>40 Spontaneous Lab Cycles</th>
<th>Studies find 15 to 40% correlation with ovulation</th>
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<tbody>
<tr>
<td>Clearblue Easy</td>
<td>Positive</td>
<td>Laboratory</td>
<td>50 Infertile Lab Cycles</td>
<td>40 Spontaneous Lab Cycles</td>
<td>Studies find 15 to 40% correlation with ovulation</td>
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<td>Positive</td>
<td>Laboratory</td>
<td>273</td>
<td>36</td>
<td>Positive test rate of 15%</td>
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3. Endometrial biopsy is useful

- Confirms ovulation and allows dating
- Detects rare subclinical endometritis

- But
  - Pain
  - Cost
  - Poor reproducibility
    - Same slide, same pathologist - 24% agreement
    - Can’t do in conception cycle
  - SHOULD NOT BE ROUTINE!
Submyth: “Day 21” Progesterone should be measured
- Don’t rely on the calendar
- Day 10 – 12 follicle check
- LH kit
- Measure Prog 8 days after surge
- If P4 > 2.0 ng/mL, patient ovulated

Progesterone levels
- Nat cycle 10
- Clomid cycle 15
- Pregnancy 10-20 controversial

Progesterone supplementation: no PO!
- Prometrium gelcaps: 200-400 bid
- Endometrin tablets: 100 tid (100/200)
- Compounded suppositories: 400 mg bid
- Crinone 8% adhesive cream 90 gm qam
- Progesterone in oil 50 mg IM daily
- Stop at 10 weeks if not bleeding
- Wean slowly to 12 weeks if some bleeding

4. Sonograms are not routine
- Fertility evaluation
- Natural Timed Intercourse
- Clomid Timed Intercourse
- Assessment of cysts
- Assessment of fibroids
- Assessment of pain
- Suspicion of endometriosis
- Diagnosis of hydrosalpinx

Fertility Evaluation
- Dx: Fertility testing (V26.21)
- Day 3 FSH/E2
- Day 3 Sonogram (baseline)
- Day 5-10 HSG
- Semen analysis any time in cycle
- Day 10 – 12 Sonogram (follicle check)
- Day “21” Progesterone
- CPT: 76830
**Natural Timed Intercourse**

- DX: Unexp Infertility (628.9 or V26.1)
- Day 3 FSH/E2 + Sono (76830)
- Day 10 – 12 Follicle check
- Clear Blue Digital
- TIC qday when smiling 😊
- +/- Prog

**Clomid Timed Intercourse**

- DX: 256.4 (PCO) vs 628.0
- Day 3 FSH/E2/HCG + Sono
- Day 10 – 12 Follicle check Sono
- Repeat Follicle check Sono in 3 – 4 days
- LH kit when follicle > 14mm
- TIC❤️
- Check Prog in 1st cycle
- Patient should be referred if not pregnant after 3 cycles

**Half Time Highlights**

- Day 3 FSH has limitations
- BBTs are not accurate
- LH kits work well
- Endometrial Bx is not useful
- Day 21 Progesterone shouldn't always be measured
- One sonogram is never enough

**5. Infertility is a woman’s problem**

- [Image of a sperm]

**Sperm**

Semen analysis (WHO)
- Concentration: >15 mill/ml
- Motility: >60%
- Morphology: >30%WHO
- >14% strict
- <4% ICSI

**6. Infertility is not covered**

Is infertility covered? A Quiz

- Not at all
- Sometimes
- Most of the time
- All of the time
Submyth: All infertility treatments are expensive

- IUIs are hundreds of dollars
- IVF is about $10000-$15000
- IVF costs have not changed significantly in 20 years
- IVF success rates have improved 4-fold in some centers

Why is IVF expensive?

<table>
<thead>
<tr>
<th></th>
<th>CPT Code</th>
<th>Description</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ov/Sonos/Bloods</td>
<td>76830/99213</td>
<td>$1608</td>
<td></td>
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<tr>
<td>Complex prep w/ SA</td>
<td>89263</td>
<td>$378</td>
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<tr>
<td>Oocyte Identification</td>
<td>89254</td>
<td>$2002</td>
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<tr>
<td>Retrieval</td>
<td>58720</td>
<td>$1550</td>
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</tr>
<tr>
<td>Anesthesia</td>
<td>00940</td>
<td>$640</td>
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<tr>
<td>US guidance @ Retrieval</td>
<td>76948</td>
<td>Included</td>
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<tr>
<td>Transplantation of oocytes</td>
<td>89268</td>
<td>$250</td>
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<tr>
<td>Culture of embryos</td>
<td>89250</td>
<td>Included</td>
<td></td>
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<tr>
<td>Embryo prep for transfer</td>
<td>89255</td>
<td>Included</td>
<td></td>
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<tr>
<td>Embryo transfer with ultrasound</td>
<td>58974</td>
<td>$1850</td>
<td></td>
</tr>
<tr>
<td>Trail transfer</td>
<td>76942</td>
<td>$165</td>
<td></td>
</tr>
</tbody>
</table>

Total Cost = $8474

Micromanipulation Table

PGD - Abnormal Embryo
7. You can’t do IVF without breaking a few embryos
   - Vitrification: Egg freezing allows the successful freezing of unfertilized eggs
   - It is possible to limit the number of eggs that are fertilized and freeze the remainder of unfertilized eggs
   - Vitrification is new, but becoming mainstream

8. IVF causes multiple births
   - SET pregnancy rates approach pregnancy rates of 2 or 3 embryos
   - In women under 40, there is virtually no difference in pregnancy rates between transfer of 2 vs 3 embryos in our lab
   - Scott, et al compared SET 41% PR vs SET + chromosomal analysis 55% PR

9. IVF causes autism
   - Danish study Hvidtjorn et al 1995-2003
   - 588,967 children
   - 5.6 % born from ART. 0.68% with ASD
   - Natural conceptions 0.61% with ASD
   - Statistically significant!
   - But significance disappears when controlling for parental age

10. All IVF Docs are the same
    - Survey of 591 new patients (1/09)
    - 81 IVF recommended (14%)
    - 510 Dx or OI/IUI
    - Most patients don’t want or need IVF
    - The best IVF Doc knows when not to do IVF

Outreach sites
The top ten myths

- Day 3 FSH is helpful in some cases
- LH kit is the best way to predict ovulation
- Endometrial biopsy is no longer useful
- One sonogram is never enough for evaluation
- Infertility is a couple’s problem
- Infertility is sometimes covered and has remained the same cost for 20 years
- Vitrification allows IVF without freezing or excess embryos
- IVF prevents multiple births
- IVF does not increase risk of autism, and PGD decreases risk of genetic disease
- The best infertility docs offer the easiest cheapest treatment that works for the patient